<u>IN THE DRAWINGS</u>:

Figure 1 has been amended as shown on the Replacement Sheet attached hereto.

REMARKS:

The present amendment revises the title, specification, drawings and claims to conform the present PCT application to the requirements of United States patent practice. The cancellation of claims 1-26 in favor of the claims presented herein has been done solely because the amount of bracketing and underlining that would have been necessary to conform claims 1-26 to the requirements of United States patent practice would have been unduly burdensome and confusing. No change in the claim language has been made for distinguishing any of the claims over the teachings of the prior art of record. Accordingly, no change in the claim language is considered by the Applicants as a surrender of any of the subject matter encompassed within the scope of the original claims.

Early consideration of the application on the merits is respectfully requested.

Submitted by,
Steven H. Noll (Reg. 28,982)
Schiff, Hardin LLP
CUSTOMER NO. 26574
Patent Department
6600 Sears Tower
233 South Wacker Drive
Chicago, Illinois 60606
Telephone: 312/258-5790
Attorneys for Applicant(s).

CH1\ 4403681.1

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10/562302
IAP17 Rec'd PCT/PTO 22 DEC 2005

~~DETECTION OF DIASTOLIC HEART FAILURE~~

~~Technical Field~~

SPECIFICATION

TITLE

"APPARATUS FOR DETECTING DIASTOLIC HEART FAILURE

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to an implantable medical apparatus for detecting diastolic heart failure, DHF, ~~comprising~~ of the type having a DHF determining device for determining at least one DHF parameter for detecting a DHF state of the heart of a patient. The invention also relates to a pacemaker having such an apparatus, and a method for detecting diastolic heart failure, DHF, ~~comprising~~ including the step of determining at least one DHF parameter for detecting a DHF state.

~~Background~~

Description of the Prior Art

There is a growing recognition that congestive heart failure caused by a predominant abnormality in the diastolic function, i.e. diastolic heart failure, DHF, is both common and causes significant morbidity and mortality. Therefore early detection of DHF is important such that a suitable treatment can be started. Patients do not, however, seem to have symptoms at an early stage. In addition it has been hard to separate diastolic and systolic heart failure and they may also exist simultaneously.

The time progress of different phases of diastole of a patient suffering from DHF is changed vis-à-vis that of a healthy person, see Michael R. Zile and Dirk L. Brusaert, "New Concepts in Diastolic Dysfunction and Diastolic Heart Failure: Part I", Circulation 2002; 105: 1387. Thus DHF can be divided into three phases, see figure 1. Figure 1 a shows left atrial pressure, LA

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dotted line, and left ventricular pressure, LV solid line, as functions of time for a normal, healthy state and for three phases of DHF. The first phase of DHF is referred to as "Impaired Relaxation". In this phase characteristic times related to relaxation and filling of the left ventricle is prolonged compared to corresponding times of a normal heart. After this phase the disease progresses into a phase called "Pseudonormal". In this phase the heart compensates and the characteristic times returns to more normal values, close to those of the normal heart. This phase is followed by the final phase of DHF called "Restrictive". In the final phase the characteristic times are shorter than for the normal heart. Figure 1b shows corresponding measured mitral blood flow velocities. Letter "E" denotes the so-called E-wave, early filling of the ventricle, and "A" the A-wave, contribution from the atrium during its contraction.

SUMMARY OF THE INVENTION

~~The purpose~~ An object of the present invention is to utilize these changes in time during diastole of patients suffering from DHF for proposing a technique for DHF detection.

~~Disclosure of the Invention~~

~~This purpose is obtained by an apparatus, a pacemaker and a method of the kind mentioned in the introductory portion of the description and having the characterizing features of claims 1, 17 and 18 respectively.~~

The above object is achieved in accordance with the present invention by an implantable medical apparatus for detecting DHF, including a sensor that interacts with a heart to obtain information associated with functioning of the heart, and a DHF determining device supplied with the sensed information that detects a DHF state of the heart from the sensed information by determining, as a DHF parameter, a time duration of a predetermined phase of diastole of the heart.

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Thus with the present invention early detection of DHF is possible and it is also possible to detect how the disease progresses. Even the beginning of a DHF of a healthy person can be detected.

~~According to advantageous~~ In embodiments of the apparatus according to the invention the DHF determining device ~~comprises~~ includes a sensor and a calculating ~~means~~ unit for determining the time, DT, from the occurrence of peak blood flow velocity through the mitral valve to zero blood flow velocity therethrough as said DHF parameter. The sensor and calculating ~~means~~ unit are adapted to determine DT by extrapolating the mitral blood flow velocity to zero, if zero velocity is not obtained before atrial contraction. The sensor and calculating ~~means~~ unit are then preferably adapted to determine the time derivative of the blood flow velocity through the mitral valve shortly after said peak blood flow velocity for use for linearly extrapolating the blood flow velocity to zero. DT denotes the E-wave deceleration time or "Dec time" related to the early filling of the left ventricle as mentioned above. If zero velocity is not obtained due to the atrial contraction, so-called A-wave influence, which will be described more in detail below. DT can consequently be determined by extrapolation in such situations.

~~According to still~~ In another ~~advantageous~~ embodiment of the apparatus according to the invention the DHF determining device ~~comprises~~ includes a sensor and a calculating ~~means~~ unit for determining isovolumic relaxation time, IVRT, i.e. the time from the closing of the aortic valve to the opening of the mitralis valve, as ~~said~~ the DHF parameter.

~~According to yet~~ In other ~~advantageous~~ embodiments of the apparatus according to the invention the sensor and calculating ~~means comprise a means for measuring~~ unit detect an IEGM or ~~a means for measuring~~ an impedance in the patient's heart or [[a]] detect sound ~~sensor~~ or activity in which case the sensor is an accelerometer[[,]]. The sensor is intended to be placed on the left ventricle of the patient's heart, for determining DT and/or IVRT. Thus e.g. IVRT can be determined from impedance measurements between the left and right ventricles, or possibly between the left ventricle and

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right atrium. Since there is no change in the blood volume between electrodes located as indicated above during IVRT, the impedance will be substantially constant. IVRT can consequently be identified as a "still" period in the impedance after systole. IVRT can also be determined by an accelerometer positioned on the left ventricle, for instance in one of the coronary veins running on the outside of the left ventricle. IVRT is then determined by the time the ventricle is still after systole, since the ventricle is still during IVRT. No blood enters or leaves the ventricle during this phase of the cardiac cycle, only a redistribution of the pressure takes place within the ventricle without change of volume of the ventricle. DT can be determined by e.g. listening to the blood flow through the ~~mitralis~~ mitral valve. The blood velocity is correlated to the frequency of the heart sound signal, its derivative corresponds to the acceleration of the blood, and DT is calculated therefrom.

~~According to~~ In other ~~advantageous~~ embodiments of the apparatus according to the invention the DHF determining device ~~is adapted to determine~~ determines the time ~~length~~ duration at predetermined time intervals and a ~~storing means~~ memory is provided for storing ~~said~~ the determined time ~~lengths~~ durations. The DHF determining device ~~can~~ alternatively can be adapted to determine changes in ~~said~~ the time ~~length~~ duration and a ~~storing means be~~ memory is provided for storing the determined changes in time ~~length~~ duration. During the follow-up of the patient stored parameters are downloaded from the ~~storing means~~ memory and are evaluated by the physician for studying the progression of the disease It is also possible to provide an alerting means ~~to be~~ that is triggered if deviations of the determined time ~~length~~ duration from predetermined limit values exceed a predetermined threshold value, or a change in the determined time ~~length~~ duration exceeds a predetermined threshold value. Thus in response to the detection of a change in the DHF parameter indicating that the patient is developing DHF or the patient is progressing into a new phase of DHF an alert can be sent calling for a follow-up by a physician.

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The invention also relates to a pacemaker provided with the apparatus for detecting DHF and a control ~~means for optimizing~~ unit that optimizes pacing therapy and pacemaker settings depending on the determined time ~~length~~ duration, as well as a method of detecting DHF.

~~Brief Description of the Drawings~~

~~To explain the invention in greater detail embodiments of the invention will now be described with reference to the drawings on which figure1a and b shows left ventricular and left atrial pressures and mitral blood flow velocity respectively for a normal heart and for three phases of DHF, figures 2 - 4 illustrate impedance measurements for determining IVRT in three embodiments of the invention, figure 5 illustrates an embodiment of the invention comprising special sensors for DT and IVRT determination, and figure 6 is a diagram illustrating when DT and IVRT values are stored for later evaluation and when a DHF alert is sent according to an exemplifying embodiment of the invention.~~

~~Description of Preferred Embodiments~~

DESCRIPTION OF THE DRAWINGS

Figs. 1a and 1b respectively show left ventricular and left atrial pressures and mitral blood flow velocity for a normal heart and for three phases of DHF.

Figs. 2, 3 and 4 respectively illustrate impedance measurements for determining IVRT in three embodiments according to the invention.

Fig. 5 illustrates an embodiment of the invention making uses of special sensors for DT and IVRT determination.

Fig. 6 is a diagram illustrating how DT and IVRT values are stored for subsequent evaluation, and the emission of a DHF alert, in accordance with an embodiment of the invention.

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DESCRIPTION OF THE PREFERRED EMBODIMENTS

Figure 1a shows left ventricular pressure, LV Press solid line, and left atrial pressure, LA Press dotted line, during diastole and figure 1b corresponding mitral Doppler left ventricular blood inflow, as measured by echocardiography, for a normal healthy heart and for three phases of diastole. Normal diastolic function is characterized by a predominant early diastolic mitral flow, E-wave, exceeding the velocity of left ventricular filling contributed by atrial contraction, A-wave in the figure. With impaired relaxation atrial contraction contributes relatively more to ventricular filling, viz. A-wave > E-wave, with prolonged deceleration of the E-wave, usually > 240 msec. This phase of DHF "Impaired Relaxation" is common with increasing age and may identify patients at risk for DHF. When ventricular diastolic pressure increases to the point where atrial contraction contributes little to the filling, the E-wave again becomes predominant but with rapid deceleration, first in a "Pseudonormal" pattern and ultimately in a "Restrictive" pattern, characterized by a high E-wave velocity of usually more than twice the A-wave velocity.

One of the time ~~lengths~~ <u>durations</u> which can be used to indicate the progress of DHF is the E-wave deceleration time, DT "Dec. Time", see figure 1b. DT is defined as the time length from the point of blood peak velocity through the mitral valve to the point of zero velocity, cf. figure 1b. If zero velocity is not reached due to the A-wave influence, DT is calculated by extrapolation as illustrated in figure 1b for the phase "Impaired Relaxation". The time derivative of the flow velocity through the mitral valve shortly after the blood flow peak velocity is determined for use for linearly extrapolating the blood flow velocity to zero. By measuring DT the beginning of a DHF and its progress can be detected.

The progress of DHF can be divided into three phases as mentioned above and each of these phases causes a change in DT, see figure 1b. The first phase of DHF is referred to as "Impaired Relaxation". During this phase DT is much longer than in a normal heart. After this phase the disease progresses into a phase called "Pseudonormal". In this phase the heart

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compensates and DT returns to more normal values, close to the DT value of a normal heart. This phase is followed by the final stage of DHF called "Restrictive". In this phase DT is shorter than DT of a normal healthy heart.

Another time ~~length which~~ duration that can be used to indicate the progress of DHF is the isovolumic relaxation time, IVRT, as mentioned above. In the "Impaired Relaxation" phase of diastole IVRT is longer than for a healthy heart, as appears from figure 1b. In the "Pseudonormal" phase the heart is compensating and IVRT returns to more normal values. In the final "Restrictive" phase IVRT is decreased to a shorter value than IVRT of the normal heart, cf. figure 1b.

A pacemaker according to the invention will preferably use its sensors for determining IEGMs or impedance measurements for measuring and calculating DT or IVRT at given time intervals, as will be described in further details below, and either store DT or IVRT or changes in DT or IVRT in the memory of the pacemaker. In the follow-up the development of DT or IVRT over time is downloaded from the pacemaker and the physician can evaluate the results and study the progression or regression of the disease.

An alerting ~~means~~ unit can also be provided to send an alert, calling for a follow-up for the patient in question, in response to the detection of a change in DT or IVRT indicating that the patient is developing DHF or the patient is progressing into a new phase of DHF.

IVRT is initiated by the closing of the aortic valve and terminated by the opening of the mitral valve. To determine when the aortic and mitral valves closes 3oand opens respectively impedance measurements or some kind of sensor can be used. Figure 2 illustrates an example of impedance measurements between left and right ventricles 1, 3. A current is supplied between the pacemaker case, schematically shown at 2, and the tip electrode 4 of a right ventricular lead 6, and the resulting voltage is measured between the ring electrode 8 of the ventricular lead 6 and the tip electrode 10 of a unipolar coronary sinus lead 12.

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Figure 3 illustrates an example wherein current is fed between the ring electrode 14 of a bipolar right atrial lead 16 and the ring electrode 20 of a bipolar scoronary sinus lead 18, and the resulting voltage is measured between the tip electrodes 22 and 24 of the right atrial lead 16 and the coronary sinus lead 18 respectively.

Figure 4 illustrates still another embodiment wherein current is supplied between the tip electrode 26 of a bipolar right ventricular lead 28 and the ring electrode 30 of a bipolar coronary sinus lead 32, and the resulting voltage is measured between the ring electrode 34 of the right ventricular lead 28 and the tip electrode 36 of the coronary sinus lead 32.

Since there is practically no change in the blood volume during IVRT between the electrodes used in the embodiments illustrated above, the impedance measured in this way is substantially constant. IVRT can consequently be identified as the "still" period in the impedance after systole.

Figure 5 illustrates an embodiment wherein a special sensor 38 is used. This sensor can be of a kind which picks up noise or registers mechanical events, such as for instance a so-called CMES-sensor, cardiac mechanical sensor. The CMES-sensor is a piezoelectric sensor the output signal of which contains a. o. pressure information. This information comprises several components, and in a certain frequency range the sensor is sensible to noise, i.e. it works as a microphone. The signal from the sensor comprises also the true pressure and its derivative. By suitable filtering of the sensor signal valve openings and closings can be detected.

The sensor 38 in ~~figure~~ Figure 5 can alternatively ~~comprise~~ be an accelerometer positioned on the left ventricle, for instance in one of the coronary veins running on the outside of the left ventricle, as shown in the figure. IVRT is then detected as the time when the ventricle is still after systole. During this time no blood leaves or enters the ventricle which consequently does not change volume.

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DT can be determined in an analogous way by impedance measurements or by noise measurements with the aid of a microphone positioned in a coronary vein as illustrated in figure 5, or positioned in the right ventricular apex. DT can also be determined by an accelerometer positioned on the outside of the left side of the heart, i.e. in the coronary sinus.

The time ~~length~~ duration used as parameter for detection of DHF can also be determined by more than one of the above described techniques.

Typical values of IVRT of a healthy person are 70 - 90 msec depending on age and other parameters, and typical values of DT of a healthy person are 160 - 240 msec. IVRT and DT values above 90 and 240 msec respectively are assumed to characterize a state of impaired relaxation, and values below 70 and 160 msec respectively are characterizing the restrictive phase of DHF. Thus an increase or decrease of IVRT and DT above or below the above mentioned limit values are indications of DHF and should therefore call for attention. This is illustrated in figure 6 which shows that time ~~length~~ duration values within the normal range are not stored, whereas time ~~length~~ duration values above or below the prescribed limit values are stored together with their times of occurrence. These measured time ~~length~~ duration values outside the normal range can also be triggering an alert.

The amount of deviation of the measured time lengths above or below their respective limit values is an indication of the severity of the DHF.

Thus, if the IVRT and DT values fall outside their respective normal ranges these values are stored together with the amounts by which the time lengths exceed or are below the respective limit. Possible erroneous measurement values are filtered out, such that single or very few time ~~length~~ duration values outside the normal ranges should not result in a DHF detection, and not trigger ~~a possible~~ an alert.

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~~CLAIMS~~

WE CLAIM AS OUR INVENTION:

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ABSTRACT

ABSTRACT OF THE DISCLOSURE

An implantable medical apparatus for detecting diastolic heart failure, DHF, ~~comprises~~ has a DHF determining device for determining at least one DHF parameter for detecting a DHF state of the heart of a patient. The DHF ~~determining devices comprises a means~~ includes circuitry for determining, as ~~said~~ the DHF parameter, the time ~~length (DT,IVRT)~~ duration of a predetermined phase of diastole. A pacemaker ~~comprises~~ has such an apparatus and a control ~~means for optimizing~~ unit that optimizes pacing therapy and pacemaker settings depending on the determined time ~~length~~ duration. A corresponding method of detecting diastolic heart failure, DHF, ~~comprises the step of~~ includes determining at least one DHF parameter for detecting a DHF state of the heart of a patient. ~~This step comprises determining, as said~~ As the DHF parameter, the time ~~length (DT,IVRT)~~ duration of a predetermined phase of diastole is determined.

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